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Trichoderma fungaemia in a neutropenic patient with pulmonary cancer and human immunodeficiency virus infection

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A 58-year-old man who has been infected with human immunodeficiency virus (HIV) since 1986 presented with fully suppressed plasma HIV replication while undergoing combination antiretroviral therapy, and with a persistent cellular immune deficiency (CD4 cell count = 212/mm^3). In 2005, he had been diagnosed with bronchopulmonary adenocarcinoma (T2N0M0), and a lobectomy was undertaken and adjunctive chemotherapy was given. At first tumour relapse in 2006, he was treated with three cycles of chemotherapy and radiotherapy. In March 2007, a second relapse was diagnosed, and treatment with carboplatine, vinorelbine and steroids (solumedrol 120 mg at day 1 and oral methylprednisolone 40 mg at day 2) was initiated on 13 April. After the first treatment cycle, the patient presented with a febrile aplasia, and co-amoxiclav and ofloxacin were prescribed. A second chemotherapy cycle was completed on 22 May, and on 25 May, the patient presented with a 1-day history of fever, chills and abdominal pain. Upon admission, his temperature was 38.5°C, his heart rate was 130 beats/min and his blood pressure was 130/80 mmHg. Clinical examination revealed a generalized abdominal tenderness and diarrhoea, as well as severe leukopenia (leukocyte count, 300/mm^3; neutrophil count not performed) and anaemia. Urine culture remained sterile. Chest X-ray showed no infiltrate. Treatment with broad-spectrum antibiotics was initiated (piperacillin–tazobactam and amikacin). Blood cultures obtained from both the central venous catheter (a long-duration chamber catheter had been in place since 2006) and a peripheral vein upon admission yielded wild-type *Escherichia coli*, suggesting intestinal translocation. On day 5 after admission (30 May) the neutrophil count rose above 500/mm^3, and treatment with piperacillin–tazobactam was replaced by treatment with amoxycillin for a total duration of 9 days. One blood culture (using BacT/Alert; BioMérieux, Lyon, France) of a sample drawn at admission (25 May) from a peripheral vein yielded a mould identified as *Trichoderma longibrachiatum*.

Identification was confirmed by DNA amplification and sequencing of a fragment, including the 3'-end of the 18S rRNA gene, internal transcribed spacer (ITS)-1, the 5.8S rRNA gene, ITS-2, and the 5'-end of the 28S rRNA gene (ITS-1–ITS-2) (National Reference Centre for Mycoses, Institut Pasteur, Paris).

The same mould was isolated from two additional blood cultures (three positive blood cultures in total) drawn from the central venous catheter on 28 and 31 May, whereas the matching blood cultures drawn from peripheral veins remained negative. Intravenous antifungal therapy was initiated with amphotericin B (1 mg/kg/day) on 31 May, and the central venous catheter was removed on 1 June.

Cultures of both the distal catheter tip and the catheter body, as well as of sputum, urine and stools, were negative for *Trichoderma*. High-resolution computed tomography scans (both chest and abdominal) showed no sign of abscess or fungal dissemination. A computed tomography scan of the nose and sinuses showed focal thickening of the mucosa of the left maxillar sinus, without signs of sinusitis. MICs determined according to EUCAST guidelines (http://www.escmid.org/Files/EUCAST%20moulds%20discussion%20document_071019.pdf) were as follows: amphotericin B, 1 mg/L; fluconazole, ≥64 mg/L; itraconazole, 2 mg/L; voriconazole, 0.5 mg/L; posaconazole, 4 mg/L; and caspofungin, 0.5 mg/L. These results were in accordance with those of others [1,7,8,10]. After 7 days of empirical treatment with amphotericin B, treatment was switched to oral voriconazole (400 mg twice-daily on day 1, and then 200 mg twice-daily) for 2 months, this treatment option being confirmed *a posteriori* as the best option in this case. All subsequent blood cultures remained sterile, and no relapse of *Trichoderma* infection was observed after discontinuation of voriconazole and at follow-up 4 months later.

In summary, *Trichoderma* spp. are ubiquitous filamentous fungi that are rarely responsible for human infections [1]. Contamination is mostly air-related, but exposure to contaminated water or food could also be responsible [2]. Five species of *Trichoderma* have been identified as human pathogens: *T. longibrachiatum*, *Trichoderma harzianum*, *Trichoderma koningii*, *Trichoderma pseudokoningii* and *Trichoderma viride*. *T. longibrachiatum* is the species most commonly encountered in the case of invasive infections. *Trichoderma* infections have been reported in patients undergoing immunosuppressive therapies (chemotherapy for solid tumours, haematological malignancies, and after bone marrow or solid organ transplantation) and in patients with peritoneal dialysis. Among the 23 cases reported in the literature so far, infections included sinusitis, necrotizing stomatitis, abcesses (pulmonary, brain or liver), ileocolic infections, catheter-induced ulceronecrotic skin infections, peritonitis in patients undergoing peritoneal dialysis, and patients with disseminated infections [1–9]. Reported mortality rates are as high as 50%. Diagnosis relies on positive cultures from involved organs or skin biopsy specimens, and positive blood cultures have very rarely been reported, even in disseminated infections.

This unusual case of *Trichoderma* fungaemia, without any sign of pulmonary or identified deep focus infection or any identification of portal of entry, is, to our knowledge, the first such case reported to have been resolved by treatment with amphotericin B and voriconazole . Despite negative catheter culture, the catheter remains the most likely portal of entry in this case, as no deep focus of infection was identified; and among the three blood cultures positive for *Trichoderma*, the last two were drawn from the catheter, whereas matching blood cultures drawn from peripheral veins were negative. Although correlation between *in vitro* susceptibility results and clinical response remains uncertain for moulds, determination of MICs should be performed in cases of unusual fungi in order to detect high MICs [11,12].

In the present case, chemotherapy-induced neutropenia, associated with HIV-induced cellular immunodeficiency, placed the patient at risk for mould infection. Prompt diagnosis of this fungal infection, rapid initiation of antifungal therapy, and perhaps also the removal of the catheter, led to a favourable outcome.

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TRANSPARENCY DECLARATION

No dual or conflicting interest to be stated for any of the authors.

M. Lagrange-Xélot[1,2], F. Schlemmer[1], S. Gallien[1,2], C. Lacroix[2,3] and J. M. Molina[1,2]*

[1]Department of Infectious Diseases, [2]University of Paris Diderot and [3]Department of Parasitology and Mycology, Hôpital Saint Louis, Assistance-Publique Hôpitaux de Paris, Paris, France

*E-mail: marie.laxe@gmail.com

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